RESEARCH ARTICLE

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The preparation, execution and suppression of copied movements in the human brain

Abstract We used positron emission tomography (PET) to measure movement set-related changes in regional cerebral blood flow (rCBF) when human subjects were asked to copy hand movements. Movement set-related activity in the brain is thought to reflect the processes of movement selection, preparation and inhibition. Four conditions were used. In the first condition, prepare and execute (PE), the hand stimulus to be copied was shown to subjects 3 s before an auditory "go"-cue instructed subjects to execute the movement; a large part of the scanning time was therefore spent in preparing to move. In the immediate execution condition (E), the hand stimulus and the go cue were presented simultaneously. The prepare-only condition (P) was similar to PE, except subjects only prepared to make the movement and did not actually execute any movement when they heard the auditory go-cue. The same stimuli were presented in a baseline condition (B), but the subjects were instructed to neither prepare nor execute movements. There were 5 principle findings: (1) In contrast to a previous study of human set-related activity in which movements were instructed by an *arbitrary* pattern of LEDs, preparing to make a *copied* movement causes rCBF changes in area 44 in posterior Broca's area; (2) set-related activity can be recorded in the cerebellar hemispheres and midline; (3) we confirmed that the supramarginal gyrus has a general role in preparing movements – there was more rCBF in the P than the E condition; (4) the cerebellar nuclei and the basal ganglia may be particularly involved in the initiation and execution of a planned movement; these regions were more active in the PE condition than the P condition; (5) the ventrolateral prefrontal cortex and a left anterior cingulate area are part of a distributed system involved in the suppression of a motor response; these areas were significantly more active in the P than the PE condition.

Key words Broca's area · Ventral prefrontal cortex · Supramarginal gyrus · Cingulate · Cerebellum · Human

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Introduction

Motor preparatory activity has been investigated in neurophysiological studies of the non-human primate. The paradigms usually involve an initial precue that informs the monkey which movement it will have to perform when a "go" cue is presented a short time subsequently. Single-unit activity recorded after the presentation of the precue and before the presentation of the go cue, referred to as "set activity", has been argued to reflect motor planning and programming and possibly the suppression of automatically triggered movements (Wise and Mauritz 1985). Set-related activity has been recorded in the cortex in: the dorsal lateral premotor cortex (PMd; Weinrich and Wise 1982; Weinrich et al. 1984; Godschalk et al. 1985; Wise and Mauritz 1985; di Pelligrino and Wise 1991, 1993; Boussaoud and Wise 1993a, b; Riehle et al. 1994; Riehle and Requin 1995; Kalaska and Crammond 1995; Crammond and Kalaska 1996; Johnson et al. 1996); the supplementary motor area (SMA) and the pre-SMA (Alexander and Crutcher 1990a, b; Matsuzaka et al. 1992; Romo and Schulz 1992); Brodmann area 5 (Riehle et al. 1994; Kalaska and Crammond 1995; Riehle and Requin 1995); middle intraparietal (MIP; Johnson et al. 1996); the anterior cingulate cortex (Shima et al. 1991); the ventral prefrontal cortex (Boussaoud and Wise 1993a, b); and to varying degrees in various parts of the primary motor cortex (M1; Alexander and Crutcher 1990a, b; Smyrnis et al. 1992; Ashe et al. 1993; Riehle et al. 1994; Riehle and Requin 1995; Johnson et al. 1996). Most studies of

subcortical motor activity have focused on the striatum (Alexander and Crutcher 1990a, b; Apicella et al. 1991, 1992; Schultz and Romo 1992; Jaeger et al. 1993), while less attention has been paid to the possibility that set activity might also be present in the cerebellum (Thach 1978; Chapman et al. 1986).

The presence of motor set-related activity in the human brain has recently been demonstrated with positron emission tomography (PET) by Deiber et al. (1996). Deiber et al. employed a similar paradigm to that used with non-human primates. Although subjects only made a few overt movements to go cues during the minute of scanning, they spent a large part ot the scan time preparing to make movements instructed by prior precues; changes in regional cerebral blood flow (rCBF) therefore largely reflect preparatory set activity processes. Deiber et al. (1996) made two important findings: First, set-related activity was confirmed in the lateral premotor cortex, on the border between the SMA and the pre-SMA, anterior cingulate area 32, supramarginal gyrus area 40, the striatum and the thalamus. Despite this, activity in the SMA, premotor cortex, cerebellum, and cingulate cortex was still present in a condition with the same movement selection and execution requirements but which gave the subjects no opportunity to prepare. Second, they found some support for the hypothesis that different modes of movement selection depend on different premotor areas (Passingham 1993); freely selected movements, as opposed to movements instructed by arbitrary cues (the configuration of a set of light stimuli), have a greater dependence on medial premotor areas including the pre-SMA and area 32 and on prefrontal areas 9 and 10.

The present study employs a similar paradigm to look further at set-related activity. There are, however, three important differences between the present study and the previous study. First, we employed an additional condition which required subjects to just prepare movements when shown precues without subsequently executing any movement. The previous demonstration of preparatory-related changes in rCBF (Deiber et al. 1996) were made by comparing a condition that involved both preparation *and execution* with a baseline that involved neither; the possibility remains that some activity changes partly reflected execution as opposed to preparation. In the present study, any change in rCBF in the "prepare and execute" (PE) condition that genuinely reflexts preparatory planning (Mauritz and Wise 1985) should also be present in the "prepare-only" (P) condition. Greater rCBF in the PE condition than in the P condition would indicate an area primarily concerned with movement execution. Greater rCBF in the P condition than in the PE condition would indicate a region where set activity was particularly related to inhibitory processes (Wise and Mauritz 1985).

Second, the present experiment uses a different mode of movement instruction; pictures of a hand, as opposed to arbitrary LED patterns, we used to indicate which movement the subjects were to make; we refer to this process as "movement copying". There has been some sup-port for the hypothesis that medial and prefrontal areas are concerned with the free selection of actions in the absence of instructions (Deiber et al. 1991; Passingham 1993; Chen et al. 1994; Thaler et al. 1994; Jahanshahi et al. 1995), while PMd is more concerned with movements selected on the basis of arbitrarily associated instructions (Kurata 1993; Mitz et al. 1993; Passingham 1993; Kurata and Hoffman 1994; Chen and Wise 1995). Recently it has been suggested that macaque area F5 in the more ventral lateral premotor cortex (PMv) may play a particular role in comprehending the movements of other individuals (di Pelligrino et al. 1992; Gallese et al. 1996; Rizzolatti et al. 1996a, b). Movements selected by copying may therefore additionaly depend on this region. If this is the case then we should expect to record rCBF changes in the human homologue of F5 in the present study despite the absence of any ventral premotor changes under otherwise similar conditions in the earlier experiment of Deiber et al. (1996).

The third important aspect of the present investigation was the position of the scanner. In the present experiment, the field of view of the scanner was positioned so as to enable us to image all of the cerebellum. The set-related activity of the cerebellum has received comparatively little attention in non-human primates (Thach 1978; Chapman et al. 1986), despite its activation in PET experiments that involve motor imagery in the absence of overt movement execution (Decety et al. 1994). The lower position of the scanner, however, meant that we were not able to image the activity in the SMA and PMd. The benefits of being able to scan the cerebellum outweight the cost of not being able to scan the SMA and the PMd given that a number of previous investigations have already established set-related activity in these areas (Alexander and Crutcher 1990a, b; Decety et al. 1992; Matsuzaka et al. 1992; Romo and Schulz 1992; Kawashima et al. 1994; Deiber et al. 1996).

Materials and methods

Subjects

Eight normal male subjects with a median age of 30 years (range 27–52 years) were studied. All subjects were right-handed as tested by the Edinburgh Handedness Questionnaire (Oldfield 1971). The study involved the administration of 4.8 mSv effective dose equivalent of radioactivity per subject and was approved by the Administration of Radioactive Substances Advisory Committee of the Department of Health of the UK. Subjects gave informed written consent. The study was approved by the research ethics committee of the Royal Postgraduate Medical School, Hammersmith Hospital, London.

Data acquisition

Magnetic resonance imaging (MRI) scans were taken for all subjects to obtain T1-weighted spin-echo images. Subsequently 12 PET measurements of rCBF were obtained at 10-min intervals using a bolus injection technique with $H_2^{15}O$ as a tracer and a CTI 953B-PET scanner with collimating senta retracted. With a field of view of 10.8 cm in the z-plane, the subjects were positioned so as to include

all of the cerebellum. After normalization, the PET data set extended from −50 mm below the AC-PC line to approximately +60 mm above it.

Experimental design

There were four conditions, each repeated three times. In all conditions the subjects viewed a drawing of a right hand on a screen. Their right hand rested on a keypad with keys for index, middle, ring and small finger. In conditions E, PE and P, subjects executed and/or prepared to execute finger movements that corresponded with pictures of hands presented on a computer screen. When the nail of a finger in the picture was darkened, subjects prepared and/or executed a key press with their own corresponding finger. The task is clearly different from previous studies of movement selection where arbitrary stimuli such as LED patterns or auditory tones are used to instruct movements. We therefore refer to the task as a "movement copying task."

Execute immediately

One of the fingernails of the fingers in the picture on the monitor was briefly darkened (700 ms). Simultaneously with the marking of the finger, a tone was presented. Subjects were asked to respond as quickly as possible by moving the finger of their right hand that corresponded to the marked finger. The interval between trials varied between 2 and 10 s so that subjects could not predict the time of the next trial. Thus between trials they could not prepare to move a specific finger or get ready to respond at a specific time. Subjects made a total of 16 movements during the scanning period.

Prepare and execute

The PE condition used identical stimuli, but there was now a 3-s interval between the onset of the selection cue (fingernail darkening for 700 ms) and the go cue (tone). The subjects were asked to prepare to move the appropriate finger when they saw the selection cue, but not to execute the movement until they heard the tone. The time intervals between trials were constant at 5.5 s. Thus, within a trial, the subjects prepared to move a specific finger and could get ready to respond at a specific time. As in condition E, 16 movements were executed during the scanning period.

Prepare only

The condition was almost identical to PE; subjects were asked to prepare movements corresponding to those indicated by the same cue as before – darkening of the fingernail. On this occasion, however, the subjects did not make any overt movement when they heard the tone had acted as a god signal in the PE condition.

Baseline

The same visual cues, fingernail darkening, and the same auditory go cues as presented in the experimental conditions were also used in the B condition. Subjects saw the hand stimuli and heard the go signals, but they were instructed to neither prepare nor execute movements.

All subjects were pretrained immediately before scanning. Training consisted of three trials of each condition and lasted a total of 35 min. All subjects were confident that they were able to do the task. Detailed instructions of what to do in the relevant condition were repeated before each scan. In conditions PE and P, the subjects were trained to direct their attention to the "feel" of the movement they were preparing to discourage them from verbally encoding the movement. After scanning, all subjects were interviewed about their performance: (1) Which condition did youg find most difficult to perform? (2) Did you find P more difficult to do than PE? (3) Did you use verbal strategies in preparing a finger?

The reaction times of movements to the tone were recorded in conditions E and PE. To assess differences in performance of E and PE, a paired *t*-test of each subject's mean reaction time for conditions E and PE was carried out.

Data analysis of PET data

This was performed on SUN SPARC 20 work stations (SUN Microsystems, Surrey, UK) using the statistical parametric mapping software package SPM-96 (Wellcome Department of Cognitive Neurology, London, UK). PET images were realigned with the individual's MR image. PET and MR images were then normalized to the standard stereotaxic space as defined by the Montreal Neurological Institute (MNI; Evans et al. 1991, 1993). The rCBF images were smoothed with a filter of 12 mm to attenuate high-frequency noise, thus increasing the signal-to-noise ratio. Differences in global blood flow between subjects and conditions were removed by analysis of covariance. The following planned comparisons were carried out:

A. P versus B
B. PE versus B
C. E versus B
D. P versus E
E. PE versus E
F. P versus PE
G. PE versus P

Using the *t*-statistic on a voxel-by-voxel basis, SPM-*t*-maps were generated with areas of activation of $P<0.001$ – a more detailed account of the statistical analysis is given by Friston et al. (1995).

The analysis was carried out on the group of eight subjects. In order to validate the anatomical assignment of activations, we also examined individual subject data coregistered onto the individual's MRI scans.

Results

Behavioural data

Analysis of the subjects' reaction times demonstrated that subjects were able to use the advance information in the precues in the PE condition to plan or pre-programme the movement before its execution on the presentation of the go cue; reaction times were significantly faster in PE than in the "immediate execution" (E) condition ($t=8.76$, $df=7$, $P<0.0001$). The reaction times in E and PE are shown in Fig. 1.

The subjects responses to the questions posed before scanning revealed their unanimous confidence in their ability to prepare movements without executing them (P). They reported a similar subjective feeling during preparation in both the P and the PE conditions. In response to the post-scanning questions, three of eight subjects said that condition P was the most difficult to perform, and five said that E was the most difficult to perform (question 1); seven of eight said that P was more difficult than PE, and one said that PE was more difficult than P (question 2), they were unanimous in not having used any verbal strategies in preparing finger movements (question 3).
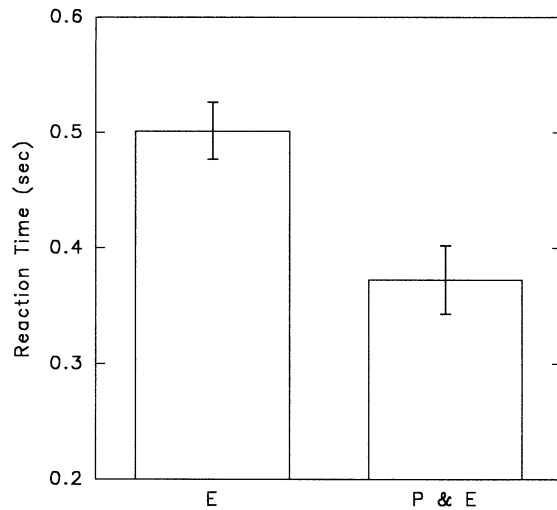
Fig. 1 Mean reaction times for immediate execution of the response in the "execute only" condition (*E*) on the *left* and in the "prepare and execute" (*PE*) condition on the *right*. *Error bars* SE of reaction time

PET data

Comparison of rCBF in experimental conditions compared with baseline rCBF

Table 1 summarizes increases in activity when each of the three conditions (P, PE, E) are compared with the baseline. Comparisons of P baseline and PE baseline revealed bilateral changes in rCBF areas 44 and 40 and the cerebel-

lum, and changes in rCBF in the left hemisphere in the premotor area 6, M1, dorsolateral prefrontal cortex (46/9) and putamen. There was additional activation in the right premotor area 6 when P was compared with the baseline. There was additional activation in the left primary somatosensory cortex (S1) and the right parieto-occipital sulcus when PE was compared with rCBF in the baseline condition. The comparison of the E and baseline conditions revealed significant rCBF changes in the lateral premotor area 6, M1, S1, putamen, thalamus, supramarginal gyrus in the left hemisphere, and the intraparietal sulcus and area 40 in the right hemisphere. Again there were significant bilateral changes in rCBF in the cerebellum.

Comparison of the conditions involving preparation, PE and P, with condition E

The comparison of conditions involving preparation, PE and P, with the E condition revealed a significant change in rCBF in a number of areas in the left hemisphere including area 44, lateral premotor area 6, and the supramarginal gyrus. There was an additional change in rCBF in the right lateral premotor cortex when P was compared with E. There was an additional change in rCBF in the left putamen when PE was compared with E. These results are summarized in Table 2.

Table 1 Regions with significant differences ($P<0.001$) in adjusted rCBF for prepare-only (*P*) prepare and execute (*PE*) and immediate execution (*E*) versus baseline (*B*) tasks. Coordinates are in standard stereotaxic space as defined by the MNI (*BA* Brodmann area)

Anatomical region	P vs B		PE vs B		E vs B	
	(Coordinates)	Z	(Coordinates)	Z	(Coordinates)	Z
Left BA 46/9	−38 +30 +34	4.32	−42 +32 +36	3.87	n.s.	
Left BA 44	−42 +06 +04	4.47	−64 +02 +08	5.19	n.s.	
	−58 +02 +28	4.12	−64 +06 +20	4.32		
Right BA 44	+48 +06 +04	3.72	+50 +04 +06	3.90	n.s.	
Left lateral premotor BA 6	−38 −06 +56	3.91	−44 −06 +56	4.21	−34 −08 +60	4.21
Right lateral premotor BA 6	+50 −08 +50	3.84	n.s.		n.s.	
Rostral cingulate area	−02 +02 +54	3.30	−02 +02 +54	5.06	−02 +02 +54	3.88
Left M1	−28 −18 +64	3.69	−30 −22 +64	4.37	−42 −18 +56	3.48
Left S1	n.s.		−32 −34 +50	4.07	−34 −36 +50	4.18
Right M1	+58 −16 +44	4.29	n.s.		n.s.	
Left putamen	−28 −02 +14	3.76	−32 −12 −02	4.09	−28 00 +12	3.37
Left thalamus	n.s.		n.s.		−14 −16 +04	3.90
Left superior temporal gyrus	−58 −32 +20	5.09	−68 −40 +18	4.54	n.s.	
Left supramarginal gyrus	−48 −34 +36	5.22	−48 −32 +34	6.46	−48 −32 +34	3.75
Right supramarginal gyrus	+60 −46 +30	3.48	+58 −44 +32	4.54	+62 −32 +22	3.48
Right parieto-occipital sulcus	n.s.		+18 −62 +38	3.59	n.s.	
Intraparietal sulcus	n.s.		n.s.		+24 −56 +44	3.43
Cerebellum						
Right hemisphere	+30 −50 −24	5.61	+30 −50 −24	6.84	+30 −50 −28	5.36
	+44 −68 −34	3.25	+46 −46 −36	5.85		
Right lateral nuclei	n.s.		+18 −50 −38	3.84	+18 −52 −38	3.26
Left hemisphere	n.s.		−32 −50 −26	4.89	−30 −48 −26	3.83
Vermis	n.s.		+08 −62 −16	4.50	+04 −72 −14	3.49

Table 2 Regions with significant differences ($P<0.001$) in adjusted rCBF for P vs E and PE vs E. Coordinates are in MNI space

Anatomical region	P vs E		PE vs E	
	(Coordinates)	Z	(Coordinates)	Z
Left BA 44	−58 +00 +14	4.58	−62 +02 +08	5.27
	−58 +04 +24	4.10	−58 +04 +22	4.21
Left lateral premotor BA 6	−42 +08 +40	4.00	−50 −06 +56	3.52
Right lateral premotor BA 6	+48 −10 +54	3.33	n.s.	
Left putamen	n.s.		−36 −14 +00	3.51
Left superior temporal gyrus	−68 −40 +12	3.19	−68 −38 +14	3.76
Left anterior inferior parietal	n.s.		−60 −24 +42	3.86
Left supramarginal gyrus	−60 −38 +24	3.53	−62 −34 +26	3.82
Subparietal gyrus	−02 −52 +40	3.45	n.s.	

Table 3 Regions with significant differences ($P<0.001$) in adjusted rCBF for P vs PE and PE vs P tasks. Coordinates are in MNI space (*VLPFC* ventrolateral prefrontal cortex)

| Anatomical region	P vs PE		PE vs P	
	(Coordinates)	Z	(Coordinates)	Z
Right anterior cingulate sulcus BA 32/10	+14 +48 +12	3.86	n.s.	
Left anterior cingulate sulcus BA 32/10	n.s.		−10 +44 +18	3.43
Left VLPFC	−48 +34 +06	3.60	n.s.	
Right VLPFC	+58 +32 +08	3.84	n.s.	
Left lateral premotor BA 6	−40 +08 +40	4.08	n.s.	
Posterior cingulate	−04 −40 +34	3.53	n.s.	
Right M1	+48 −12 +54	3.74	n.s.	
Right putamen	n.s.		+18 +06 +00	3.61
Cerebellum				
Right hemisphere	n.s.		+48 −44 −36	4.57
Right lateral nuclei	n.s.		+18 −62 −20	4.17
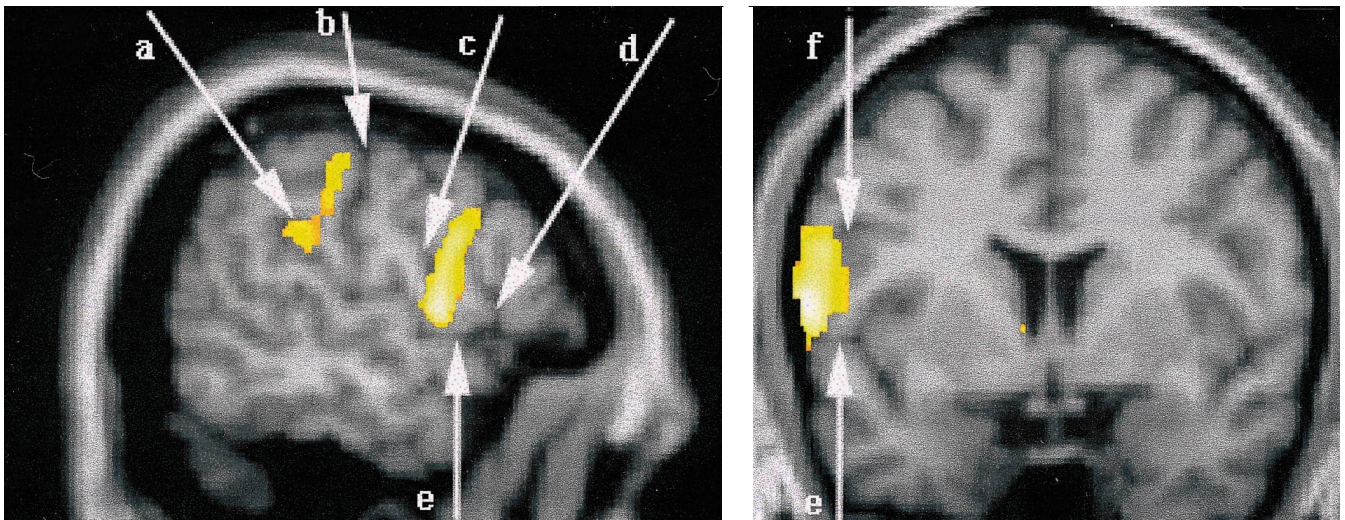
Fig. 2 *Left* Sagittal section showing the regions of significant difference in rCBF between the PE and E conditions. The difference is coregistered onto a sagittal and coronal cut of a normalized MR image in MNI space (Evans et al. 1993). One region of rCBF difference can be clearly seen in Brodmann's area 44, the pars opercularis of Broca's area which lies anterior to the inferior precentral sulcus and posterior to the ascending ramus of the Sylvian fissure. The more posterior region of rCBF change is in the supramarginal gyrus. *a*, supramarginal gyrus; *b* postcentral sulcus; *c* central sulcus; *d* ascending ramus of the Sylvian fissure; *e* Sylvian fissure. *Right* Coronal section showing the same region of significant difference in rCBF between the PE and E conditions in area 44 dorsal to the Sylvian fissure and ventral to the inferior frontal sulcus. *e* Sylvian fissure; *f* inferior frontal sulcus

Comparison of the conditions involving movement preparation either with or without subsequent movement execution

Table 3 summarizes the results of comparing the P and PE conditions. The areas of significantly greater rCBF during the PE condition than during the P condition included the the right cerebellar hemisphere and lateral nuclei and right putamen. The areas of significantly greater rCBF during the P condition than during the PE condition included the ventrolateral prefrontal cortex in both hemispheres, a region in the left anterior cingulate, a very

small area in the posterior cingulate, and the left lateral premotor cortex. No significant difference between the P and PE could be seen in the rCBF in M1.

Localization of activation in Broca's area

To investigate the exact location of activation in the region of Broca's area, we looked at changes in rCBF in single subjects co-registered with their individual MRI scans. This revealed that the inferior frontal activation was mostly anterior to the precentral sulcus and entirely posterior to the ascending ramus of the Sylvian fissure and thus appears to lie in area 44 rather than the more posterior lateral area 6. Figure 2 shows activation in ventral premotor and area 44 when comparing rCBF in the PE and E conditions.

Discussion

The paradigm

The faster reaction times of movements made in the PE than the condition demonstrate that subjects were able to use the prior information present in the precues to pre-programme movements made to the subsequent go cue. The difference in rCBF between the PE condition and the baseline may reflects structures concerned with preparation of the movements; most of the 90-s duration scan was spent in a state of preparation, during what is referred to as the "set" period in single-unit studies of motor areas, and only 16 movements were executed. A similar argument was made by Deiber et al. (1996) when they compared conditions similar to the present PE condition with a baseline condition.

It is possible to confirm that the comparison of PE with baseline does reflect preparatory activity, and not movement execution, by comparing P with the baseline; P with baseline is not confounded by any component of movement execution. A second, independent way of confirming the existence of preparation-related changes is to examine the PE and E comparison; these two conditions entailed identical movement execution components.

In summary, there are three independent methods to be used for measuring preparation-related activity in the motor system. Each comparison by itself is open to another interpretation. PE compared with baseline may reflect execution-related activity. The comparison of PE with E may be insensitive; preparatoy activity is likely to exist in brain areas concerned with movement "planning" or "selection"; the same areas must, however briefly, be activated in the E condition before the movement can be activated. The comparison of P with baseline could be criticized because, other than than the subjects' unaminous verbal report that they were able to prepare a movement that they did not subsequently execute, there is no other *behavioural* confirmation that they did prepare unexecuted movements. If the results of all three comparisons are

similar, as is the case in the present investigation, it is more parsimonious to reject these alternative interpretations and accept that the same process, preparation, is being imaged in each comparison. Only two novel areas of activation difference were found in the P–PE subtraction – the ventrolateral prefrontal cortex and the left anterior cingulate. It is argued below that the suppression of behavioural output may depend on these areas.

The difficulty of finding a behavioural index by which to assess performance in condition P is one shared with other experiments involving preparation-only conditions (Kawashima et al. 1994) and mental imagery conditions (Decety et al. 1994; Stephan et al. 1995). In the study of Kawashima et al. (1994), subjects were asked to prepare a single movement over the entire 90 s of scanning; it is arguable that the activity changes also reflect the short-term memory processes recruited throughout this time period rather than the single act of motor preparation. In the present investigation, subjects were required to prepare 16 different movements in the P condition for shorter time periods of just 3 s.

The subjects in the present experiments were simply instructed to prepare movements. The P condition could therefore be said to require just the *imagination* of the movement. The prepare conditions correspond particularly to what Jeannerod (1995) refers to as "internal", as opposed to "external" motor imagery; the subjects were asked to concentrate on the "feel of the movement" and not to verbalize the movement. Despite the recent interest in motor imagery (Jeannerod 1994, 1997; Stephan et al. 1995; Porro et al. 1996; Roth et al. 1996), Jeannerod has argued that motor imagery and motor preparation are functionally equivalent.

It has also been argued that movement imagination and movement execution depend on the same brain areas (Decety 1996). Preparation-related activity in the present experiments is therefore likely to be greatest in brain structures that operate during the normal selection and planning of immediately executed movements; the preparation conditions are therefore being used as a tool to facilitate the scanning of what might otherwise be transitory brain activity.

It should be reiterated that in order to position the scanner so as to include the whole of the cerebellum in the z-plane down to 50 mm below the anterior commissure-posterior commissure line (AC-PC line), we were not able to scan the most dorsal cortical structures. This limited our ability to image the lateral premotor cortex and the SMA in their entirety. According to Fink et al. (1997), finger-related activity is seen at heights of $46 < z < 67$ mm in the premotor cortex and $67 < z < 73$ mm in the SMA. The present results were normalized with respect to the MNI average brain template (Evans et al. 1993) and not with respect to the flatter brain used by Talairach and Tournoux (1988). PET has, however, already been used to confirm the existence of preparation-related activity in these areas (Deiber et al. 1991; Decety et al. 1992; Kawashima et al. 1994; Jahanshahi et al. 1995; Stephan et al. 1995) as might have been expected

from single-unit studies in monkeys (Weinrich and Wise 1982; Godschalk et al. 1985; Wise and Mauritz 1985; Alexander and Crutcher 1990a, b; di Pelligrino and Wise 1991, 1993; Matsuzaka et al. 1992; Romo and Schultz 1992; Boussaoud and Wise 1993a, b; Riehle et al. 1994; Kalaska and Crammond 1995; Riehle and Requin 1995; Crammond and Kalaska 1996; Johnson et al. 1996).

Broca's area

There was a significant increase in rCBF in Broca's area when either the PE or P conditions were compared with the baseline or E conditions. Broca's area, since its definition, has been associated with language; it is important to rule out the possibility that the activation is not simply in the more ventral part of area 6 in the lateral premotor cortex. The activation peaks for the group data are at MNI coordinates (Evans et al. 1991, 1993), −42, +6, +4 (P-baseline) and −58, 0, +14 (P-E); −64, 2, +8 (PE-baseline) and −62, 2, +8 (PE-E). These peaks therefore fall in the pars opercularis of the inferior frontal gyrus. The pars opercularis is delimited posteriorly by the inferior precentral sulcus and anteriorly by the ascending ramus of the Sylvian fissure and has been designated area 44 by Brodmann (Brodmann 1909; Sarkissov et al. 1955; Petrides and Pandya 1994). We also examined the position of the ventral frontal activation area with respect to the precentral sulcus on the MRI scans of individual subjects. The area of peak activity was shown to be in front of the precentral sulcus and behind the ascending ramus of the Sylvian fissure (Fig. 2). It is therefore likely to be in posterior Broca's area (area 44) as opposed to lateral area 6.

The activation of Broca's area is unlikely to be due to linguistic mediation in the task. First, there was no evidence of changes in rCBF in the region of Broca's area when subjects covertly prepared for similar durations in a previous study of a more difficult movement-selection task (Deiber et al. 1996). In that study, the finger to be moved and the direction in which it was to be moved were independently instructed by different sets of light cues. The arbitrary stimulus-response mapping and the similarity of the cue configuration for quite distinct movements in the previous studies made the process of movement selection more difficult than in the present case. Second, the increase in rCBF in area 44 was similar to that seen in the lateral premotor area 6 and the supramarginal gyrus; it was most prominent in the left hemisphere but a small increase was also seen in the right hemisphere (Table 1). Third, subjects are able to copy a movement more quickly than they are able to name it; this casts serious doubt on any suggestion that a linguistic process might intervene between the presentation of the hand position to be copied and the subjects' responses.

Instead the additional activation of area 44 in the present task is likely to reflect the distinct mechanism by which subjects selected movements in the present experiment. Petrides and Pandya (1994) have argued that hu-

man area 44 is homologous to an area they also label 44 in the posterior bank of the inferior limb of the arcuate sulcus in the macaque. Von Bonin and Bailey (1947) labelled the macaque area FCBm and considered it to be homologous to the human area FCBm of Von Economo (1929), Brodmann's area 44. Preuss (1995) has pointed out that the region can even be identified in New World monkeys and the prosimian *Galago*. In the macaque the region has also been labelled F5 (Matelli et al. 1985). Neurons in area F5 code for specific grasping movements made by the monkey (Rizzolatti et al. 1988) and also for grasping movements that the monkey observes other individuals making (di Pelligrino et al. 1992; Jeannerod et al. 1995; Rizzolatti et al. 1996a, b; Gallese et al. 1996). It has been suggested that these neurons may mediate motor imagery (Jeannerod 1994) or motor event recognition (Rizzolatti et al. 1996a). An alternative explanation is that area 44 is concerned with the planning and selection of movements that require "standard" mappings of stimulus and response. Wise et al. (1997) distinguish between standard and "non-standard" mapping. In standard mapping there is a spatial correspondence between the cue (e.g. the picture of a hand) and the response (e.g. the hand movement); in non-standard mapping the relation is arbitrary.

We do not think that the activation of area 44 in Broca's area is related to movement preparation per se; instead its activation is related more specifically to the preparation of a certain class of movements – copied movements. Other premotor and prefrontal regions are important for the selection of actions (Passingham 1993). Human and non-human primate studies involving single-unit recording, permanent aspiration lesions; temporary inactivation with muscimol and PET have shown that the PMd selects arbitrary actions (e.g. joystick movements) on the basis of arbitrary instruction (e.g. colour cues; Halsband and Passingham 1985; Deiber et al. 1991; Boussaoud and Wise 1993a, b; Kurata 1993; Kurata and Hoffman 1994; Mitz et al. 1993; Passingham 1993; di Pelligrino and Wise 1993). The dorsolateral prefrontal cortex, in conjunction with the mesial cortical motor areas, the SMA, the pre-SMA, and the cingulate cortex is important for the selection and initiation of self-paced movements in the absence of external cues or instructions (Deiber et al. 1991; Frith et al. 1991; Chen et al. 1994; Thaler et al. 1994; Jahanshahi et al. 1995). The premotor areas activated by a preparation condition depend, to some extent, on how the movement is selected; preparation which is sustained over time may be associated with similarly sustained activity in the relevant premotor structure. When movements were freely selected, as opposed to cued by an arbitrary pattern of LEDs, Deiber et al. (1996) found that preparatory activity was greater in the pre-SMA, anterior cingulate, and dorsolateral prefrontal area 9 – the same areas that have been found to be more active in previous experiments that have compared self-paced or freely selected movements with cued movements in the absence of any delay period (Jahanshahi et al. 1995; Frith et al. 1995). By the same logic, the present results

suggest that more ventrally, in area 44, there is a distinct premotor system concerned with the selection of actions on the basis of imitation. This argument is supported by a recent report by Erhard et al. (1996), who also recorded Broca's area activation in an fMRI study of movement imitation, even in the absence of a delay between cue and movement. No significant blood flow changes have been seen in this region when subjects perform similar tasks but with no element of action copying (Jahanshahi et al. 1995; Deiber et al. 1996). The PMv may be concerned with other standard sensorimotor mappings. Reaching, grasping (Gentiluci et al. 1983; Rizzolatti et al. 1983; Fogassi et al. 1992; Savaki et al. 1993; Kurata and Hoffman 1994) and movement copying all involve spatially congruent stimulus response mappings and all processes are associated with the PMv.

The existence of a distinct premotor system concerned with the selection of actions by copying is also suggested by apraxia. There is a robust dissociation between impaired movement-copying in ideomotor apraxia and impairments in miming object use and the learning of arbitrary stimulus response associations in ideational apraxis (De Renzi et al. 1968; Barbieri and De Renzi 1988; De Renzi and Lucchelli 1988; M.F.S. Rushworth et al. 1998).

Rizzolatti and colleagues (Grafton et al. 1996; Rizzolatti et al. 1996b) have recently used PET to scan subjects while they performed grasping observation tasks similar to those used in previous studies with monkeys. They compared blood flow when subjects observed objects being grasped or simply observed and recorded activation peaks in Broca's area at Tailarach coordinates −32, +34, +4 (Rizzolatti et al. 1996b) and −48, 36, 12 (Grafton et al. 1996). These foci are therefore approximately 3 cm more anterior than the one recorded in the present experiment. It is not clear exactly where the foci lie with respect to the major sulci of the inferior frontal gyrus, but they most probably fall within the more anterior area 45. Rizzolatti et al. (1996b) have discussed unpublished evidence for distinct populations of visual/complex neurons and non-visual neurons in monkey F5. It is possible that the discrepant locations of the motor-related foci in Broca's area in comparison between object grasp observation and object observation comparison (Rizzolatti et al. 1996b; Grafton et al. 1996) and the present movement imitation-hand observation comparison reflect different neuron populations. This would be consistent with the finding that activation is found more posteriorly, in area 44, when actually imaging making movements was compared with object observation (Grafton et al. 1996). Alternatively the more anterior focus recorded by Rizzolatti et al. (1996b) may not be the human homologue of the monkey F5 area, and its activation may be related to the attentional role of adjacent dorsolateral prefrontal cortex (Passingham and Nixon 1996; Rushworth et al. 1997a). A significant change in rCBF was seen in the dorsolateral prefrontal cortex when both of the conditions involving preparation, P and PE, were compared against the baseline (Table 1).

Activation has previously been recorded in Broca's area in other PET studies of motor tasks (Decety et al. 1994; Parsons et al. 1995; Stephan et al. 1995). The complicated task designs used in these experiments involved more than just movement selection and activated large regions of cortex in additional to the opercular part of Broca's area; it was therefore not possible to equate the activation of opercular Broca's area with the aspect of movement selection.

Primary motor cortex

There has been some controversy about whether or not the M1 is involved in the process of motor imagery. Motor imagery PET and fMRI studies have variously reported no activation of M1 (Rao et al. 1993; Sanes et al. 1993; Decety et al. 1994; Parsons et al. 1995), M1 activation in just some subjects (Leonardo et al. 1995; Sabbah et al. 1995; Stephan et al. 1995) or a general M1 activation during fMRI motor imagery (Porro et al. 1996; Roth et al. 1996). In the present experiment, we found activation during the P condition which only required movement preparation as opposed to actual movement execution. This result confirms that overt behavioural output is not necessary for M1 activation in PET and is consistent with Decety's (1996) suggestion that the same brain regions are involved in both motor execution and motor imagery.

It remains a possibility that the M1 rCBF changes seen in P, and in the motor imagery paradigms of other researchers, reflect presynaptic inhibition of M1. It is clear, however, that monkey M1 motor cortical cells modulate their activity in relation to the mental planning of arm movement (Georgopoulos et al. 1989) and that the excitability of specific M1 muscle representations change during human motor imagery (Fadiga et al. 1995).

Supramarginal gyrus

Changes in rCBF were recorded in the anterior supramarginal gyrus in both the PE and P conditions in comparison with the baseline and E conditions (Tables 1, 2). The area of activation included Bordmann's area 40 and was mot prominent from the end of the Sylvian fissure to the postcentral sulcus. Grafton et al. (1996) recorded changes in rCBF in the subcentral sulci in the parietal operculum by the insula in a region they suggest may be the human homologue of SII when they contrasted reaching and grasping with reaching; no rCBF changes were recorded in this region in the present study. Deiber et al. (1996) have suggested that area 40 may play a particular role in motor preparation; in comparisons against baseline, they recorded high rCBF in the anterior part of area 40 when subjects were able to prepare movements before executing them and lower rCBF when movements were executed immediately to the presentation of cues. By employing the P condition in the present study and comparing the rCBF with that recorded during the E condition, we were able to confirm the association between area 40 activation and movement preparation. Furthemore,

the present study demonstrates that the role of area 40 in movement preparation, unlike area 44, is independent of the mode of movement selection; activation changes in area 40 are seen during both when movements are selected by standard and by non-standard sensorimotor mappings.

Area 40 may be a covert motor preparation area that performs an analogous function to the covert orienting attention area in the more posterior parietal cortex (Posner et al. 1984; Corbetta et al. 1993). Covert orienting appears to be part of a process of covert preparation for oculomotor and orienting movements (Sheliga et al. 1994). Changes in rCBF, particularly in the right hemisphere, can be recorded in this region when subjects covertly prepare oculomotor movements (Corbetta et al. 1993) and lesions impair covert oculomotor preparation (Posner et al. 1984). The present study and the study of Deiber et al. (1996) demonstrate that the supramarginal gyrus is activated when subjects covertly prepare finger movements, as opposed to oculomotor movements. In addition we have previously shown that lesions that include the left supramarginal gyrus impair normal covert motor preparation (Rushworth et al. 1997b). Area 40 and the more posterior parietal region studied by Corbetta et al. (1993) may correspond to areas 7b, and 7a, respectively, in the macaque (Eidelburg and Galaburda 1984). The connections of these areas are consistent with parallel roles in covert motor preparation (or motor attention) and covert oculomotor preparation (or orienting attention); area 7a is connected with dorsal visual areas and projects to the fontal eye fields, while 7b is connected with the somatosensory system and projects to the premotor cortex (Cavada and Goldman-Rakic 1989a, b; Matelli et al. 1986). In relation to the distributed pattern of rCBF changes seen in the present experiment, it should also be noted that the macaque area 7b is also interconnected with area F5- (Cavada and Goldman Rakic 1989a, b; Matelli et al. 1986).

For the comparison between PE and E, there was also also an activation in the most anterior part of the parietal cortex (Table 2, Fig. 2). The peak may lie within the primary somatosensory cortex (SI) and within the lower part of the hand representation (−60, −24, 42). If so, this activation may reflect the fact that the subjects were instructed to "feel" the finger while they were preparing to move it. Jueptner et al. (1997) have previously reported activation of SI when subjects were instructed to attend during the intertrial interval to the finger that they were going to move on the next trial.

The cerebellum and movement preparation

In a previous study, preparatory activity was recorded in the dorsal cerebellum when subjects prepared and subsequently executed movements, but it was greater when subjects immediately executed movements in the absence of precues (Deiber et al. 1996). Deiber et al. (1996) therefore suggested that the cerebellum was particularly concerned with the immediate translation of sensory informa-

tion into a motor response. The previous study only recorded activity to a depth of −12 mm below the AC-PC line, while in the present study, by the choice of scanner position, we were able to record activity throughout the entire extent of the cerebellum. In the present study it was clear that there was a significant difference in rCBF in the right cerebellar hemisphere when either the P or the PE condition was compared against baseline. The rCBF peaks were all 20 mm or more below the AC-PC plane and would not have been detectable in the previous study.

The presence of activation in the P condition is consistent with a role for the cerebellum in the preparation of movements based on visual cues and not simply in the execution of movements (Mushiake and Strick 1993, 1995a, b). Response preparation is slowed in patients with cerebellar lesions (Jahanshahi et al. 1993). Discrete lesions placed in the lateral cerebellar nuclei in macaques prolong the reaction times of learned sequences of movements (Nixon and Passingham 1996) but have little effect on whether or not the correct movement is selected in response to a visual cue (Passingham and Nixon 1996). Significant rCBF changes in the cerebellum have previously been recorded when subjects imagine making movements (Decety et al. 1994).

This is not to say that the cerebellum is only involved in preparation for movement. There was significantly greater rCBF in the right cerebellar hemisphere and right lateral cerebellar nuclei when the PE condition was compared with the P condition (Table 3). Muscimol injections into the dentate are known to slow movement initiation even when there is no element of preparation in the testing paradigm (Mink and Thach 1991a, b).

The striatum and movement preparation

There was significantly greater activation in the putamen during conditions involving either preparation or execution (PE, P, E) than during the baseline (Table 1). The activation was greater when there was a period of preparation before execution, PE, than when execution was immediate, E, (left putamen; Table 2). This suggests a role for the striatum in selecting and preparing movements. Preparatory activity that is specific for the response type and the response goal has been recorded in the putamen (Alexander and Crutcher 1990a, b; Jaeger et al. 1993) and the globus pallidus (Mushiake and Strick 1995a, b) in single-cells studies in monkeys. The rCBF change, however, was also significantly greater in PE than P (right putamen; Table 3), suggesting that the actual initiation of the movement is also an important factor in determining striatial activation. This is also consistent with a previous cell-recording study: twice as many anterior caudate and putamen cells were found to be active when monkeys prepared to make an over movement as opposed to when they prepared to inhibit responding to a "no-go" cue (Romo and Schultz 1992). Pallidal inactivation leads to slowed response times in some, but not all, motor tasks (Mink and Thach 1991a, b; Alamy et al. 1994).

Ventral prefrontal cortex and cingulate cortex and the suppression of movements

In general, areas of rCBF increase in the P condition were a subset of the areas of increase in the PE condition; this is consistent with the subjects' claims that they were engaged in the same process of covert response preparation in both the P and the PE conditions even though they did not make any overt response in the P condition. There were, however, areas that were significantly more active in the P than the PE condition (Table 3). Two of these differences were large, in the ventrolateral prefrontal cortex and the anterior cingulate. These may reflect the fact that the subjects were required to inhibit movements to a greater extent in P than in PE. An rCBF difference in the ventrolateral prefrontal cortex was also apparent in the direct comparison of P with baseline; there was a single voxel area of significant difference at a level of $P<0.001$, but a larger area was apparent when the significance level used was $P<0.01$.

Ventrolateral prefrontal rCBF changes seen in working memory tasks are usually interpreted as reflecting a visual form specific working memory mechanism that is the counterpart of a more dorsally located spatial working memory system (Haxby et al. 1995; Baker et al. 1996; Courtney et al. 1996; McCarthy et al. 1996). Such a dichotomy has been claimed in the macaque (Wilson et al. 1993; Goldman-Rakic 1996). However, the memory demands of the two tasks in the present experiment, P and PE, are identical. Furthermore, Rushworth et al. (1997a) have recently shown that monkeys with ventrolateral prefrontal lesions are not impaired on a working memory task, visual delayed matching. They have also pointed to the fact that monkeys with this lesion are impaired on tasks in which there is no working memory component, for example simultneous visual matching (Rushworth et al. 1997a), "go/no-go" tasks (Iversen and Mishkin 1970) and visual or spatial reversals (Butter 1969). All these tasks require the animals to inhibit or change responses. Recently, Casey et al. (1996) have used fMRI to show that the ventral prefrontal cortex activation distinguishes between high- and low-performing adolescents on a go/no-go task.

Changes in the dorsal, as opposed to the ventral, prefrontal cortex were seen when either condition involving preparation, P or PE, was compared with baseline. This may reflect the subjects intention to move in a certain way at the end of the delay. It is compatible with Fuster's (1995) suggestion that the dorsal prefrontal cortex is important for prospective memory for what an individual plans to do next.

Activation of the anterior cingulate cortex has been reported when subjects have to change between responses or inhibit responses. Changes in rCBF have been recorded during performance of a Stroop task which required subjects to direct attention to an unusual stimulus dimension and the response it instructed instead of the habitual stimulus dimension and the response it instructed (Pardo et al. 1990). Both Paus et al. (1993) and Taylor et al. (1994) have also shown that the anterior cingulate is activated in tasks which require the execution of a new response and the suppression of a habitual response. Anterior cingulate activation also distinguished high- and low-performing adolescents in the recent go/no-go study of Casey et al. (1996). The location of the peaks of activation for such tasks is variable within the anterior cingulate cortex (Paus et al. 1996; Picard and Strick 1996). The present findings demonstrate that just the suppression of the standard response is sufficient to activate this particular part of the cingulate cortex.

References

Alamy M, Trouche E, Nieoullon A, Legallet E (1994) Globus pallidus and motor initiation: the bilateral effects of unilateral quisqualic acid-induced lesion on reaction times in monkeys. Exp Brain Res 99:247–258

Alexander GE, Crutcher MD (1990a) Neural representations of the target (goal) or visually guided arm movements in the three motor areas of the monkey. J Neurophysiol 64:164–178

Alexander GE, Crutcher MD (1990b) Preparation for movement: neural representation of intended direction in three motor areas of the monkey. J Neurophysiol 64:133–150

Apicella P, Scarnati E, Schultz W (1991) Tonically discharging neurons of monkey striatum respond to preparatory and rewarding stimuli. Exp Brain Res 84:672–675

Apicella P, Scarnati E, Ljunberg T, Schultz W (1992) Neuronal activity in monkey striatum related to the expectation of predictable environmental events. J Neurophysiol 68:945–960

Ashe J, Taira M, Smyrnis N, Pelizzer G, Georgakopoulos T, Lurito JT, Georgopoulos AP (1993) Motor cortical activity preceding a memorized movement trajectory with an orthogonal bend. Exp Brain Res 95:118–130

Baker SC, Rogers RD, Owen AM, Frith CD, Dolan RJ, Frackowiak RSJ, Robbins TW (1996) Neural systems engaged by planning: a PET study of the Tower of London task. Neuropsychologia 34:515–526

Barbieri C, De Renzi E (1988) The executive and ideational components of ideational apraxia. Cortex 24:535–543

Boussaoud D, Wise SP (1993a) Primate frontal cortex: effects of stimulus and movement. Exp Brain Res 95:28–40

Boussaoud D, Wise SP (1993b) Primate frontal cortex: neuronal activity following attentional versus intentional cues. Exp Brain Res 95:15–27

Brodmann K (1909) Vergleichende Lokalisationslehre der Großhirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Barth, Leipzig (Translated by LJ Garey, 1994, Brodmann's Localization in the cerebral cortex. Smith-Gordon, London)

Butter CM (1969) Perseveration in extinction and in discrimination reversal tasks following selective frontal ablations in *Macaca mulatta*. Physiol Behav 4:163–171

Casey BJ, Trainor R, Orendi J, Schubert A (1996) A functional magnetic resonance imaging study of ventral prefrontal cortex mediation for response inhibition. Soc Neurosci Abstr 22:439.1

Cavada C, Goldman-Rakic PS (1989a) Posterior parietal cortex in rhesus monkey. I. Parcellation of areas based on distinctive limbic and sensory corticocortical connections. J Comp Neurol 287:393–421

Cavada C, Goldman-Rakic PS (1989b) Posterior parietal cortex in rhesus monkey. I. Evidence for segregated corticocortical networks linking sensory and limbic areas with the frontal lobe. J Comp Neurol 287:222–445

Chapman CE, Spidalieri G, Lammare Y (1986) Activity of dentate neurons during arm movements triggered by visual, auditory, and somesthetic stimuli in the monkey. J Neurophysiol 55:203–226

Chen LL, Wise SP (1995) Neuronal activity in the supplementary eye field during acquisition of conditional oculomotor associations. J Neurophysiol 73:1101–1121

Chen Y, Thaler D, Nixon PD, Stern C, Passingham RE (1994) The functions of the medial premotor cortex (SMA). II. The timing and selection of learned movements. Exp Brain Res 102:461–473

Corbetta M, Miezin FM, Shulman GL, Petersen SEA (1993) A PET study of visuospatial attention. J Neurosci 13:1202–1226

Courtney SM, Ungerleider LG, Keil K, Haxby JV (1996) Object and spatial visual working memory activate seperate neural systems in human cortex. Cereb Cortex 6:39–49

Crammond DJ, Kalaska JF (1996) Differential relation to discharge in primary motor cortex and premotor cortex to movements versus actively maintained postures during a reaching task. Exp Brain Res 108:45–61

Decety J (1996) Do imagined and executed actions share the same neural substrate? Brain Res Cogn Brain Res 3:87–93

Decety J, Kawashima R, Gulyas B, Roland PE (1992) Preparation for reaching: a PET study of the participating structures in the human brain. Neuroreport 3:761–764

Decety J, Perani D, Jeannerod M, Bettinardi V, Tadardy B, Woods R, Mazziota JC, Fazio F (1994) Mapping motor representations with positron emission tomography. Nature 371:600–602

Deiber M-P, Passingham RE, Colebatch JG, Friston KJ, Nixon PD, Frackowiak RSJ (1991) Cortical areas and the selection of movement: a study with positron emission tomography. Exp Brain Res 84:393–402

Deiber M-P, Ibanez V, Sadato N, Hallet M (1996) Cerebral structures participating in motor preparation in humans: a positron emission tomography study. J Neurophysiol 75:233–247

De Renzi E, Luchelli F (1988) Ideational apraxia. Brain 111:1173–1185

De Renzi E, Pieczuro A, Vignolo LA (1968) Ideational apraxia: a quantitative study. Neuropsychologia 6:41–52

Eidelburg D, Galaburda AM (1984) Inferior parietal lobule: divergent architectonic asymmetries in the human brain. Arch Neurol 41:843–852

Erhard P, Kato T, Strick PL, Ugurbil K (1996) Functional MRI activation pattern of motor and language tasks in Broca's area. Soc Neurosci Abstr 22:260.2

Evans AC, Marrett S, Torrescorzo J, Ku S, Collins L (1991) MRI-PET correlation in three dimensions using a volume-of-interest (VOI) atlas. J Cereb Blood Flow Metab 11:A69–78

Evans AC, Collins DL, Mills SR, Brown ED, Kelly RL, Peters TM (1993) 3D statistical neuroanatomical models from 305 MRI volumes. Proc IEEE Nucl Sci Symp Med Imaging Conf, pp 1813–1817

Fadiga L, Fogassi L, Pavesi G, Rizzolatti G (1995) Motor facilitation during action observation. A magnetic stimulation study. Neurophysiol 73:2608–2611

Fink GR, Frackowiack RSJ, Pietrzyk U, Passingham RE (1997) Multiple non-primary motor areas in the human cortex. J Neurophysiol 77:2164–2174

Fogassi L, Gallese V, di Pellegrino G, Fadiga L, Gentilluci M, Luppino G, Matelli M, Pedotti A, Rizzollatti G (1992) Space coding by premotor cortex. Exp Brain Res 89:686–690

Friston KJ, Holmes AP, Worsley KJ, Poline JP, Frith CD, Frackowiak RSJ (1995) Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp 2:189–210

Frith CD, Friston KJ, Liddle PF, Frackowiak RSJ (1991) Willed action and the prefrontal cortex in man: a study with PET. Proc R Soc Lond B Biol Sci 244:241–246

Fuster JM (1995) Memory in the cerebral cortex: an empirical approach to neural networks in the human and non-human primate. MIT Press, Cambridge, Mass

Gallese V, Fadiga L, Fogassi L, Rizzolatti G (1996) Action recognition in the premotor cortex. Brain 119:593–609

Gentilucci M, Scandolara C, Pigarev IN, Rizzolatti G (1983) Visual responses in the postarcuate cortex (area 6) of the monkey that are independent of eye position. Exp Brain Res 50:464–468

Gentilucci M, Fogassi L, Luppino G, Matelli M, Camarda RM, Rizzolatti G (1988) Functional organization of interferior area 6 in the macaque monkey. I. Somatotopy and the control of proximal movements. Exp Brain Res 71:475–490

Georgopoulos AP, Lurito JT, Petrides M, Schwartz AB, Massey JT (1989) Mental rotation of the neuronal population vector. Science 243:234–236

Godschalk M, Lemon RN, Kuypers HGJM, Steen J van der (1985) The involvement of monkey premotor cortex neurones in preparation of visually cued arm movements. Behav Brain Res 18:143–157

Goldman-Rakic PS (1996) The prefrontal landscape: implications of functional architecture for understanding human mentation and the central executive. Philos Trans R Soc Lond B Biol Sci 351:1387–1527

Grafton ST, Arbib MA, Fadiga L, Rizzolatti G (1996) Localization of grasp representations in humans by positron emission tomography. 2. Observation compared with imagination. Exp Brain Res 112:103–111

Halsband U, Passingham RE (1985) Premotor cortex and the conditions for movement in monkeys (Macaca fascicularis). Behav Brain Res 18:269–277

Haxby JV, Ungerleider LG, Horwitz B, Rapoport SI, Grady CL (1995) Hemispheric differences in neural systems for face working memory: a PET rCBF study. Hum Brain Mapp 3:68–82

Hyvarien J, Shelepin Y (1979) Distribution of visual and somatic functions in the parietal associative area of the monkey. Brain Res 169:561–564

Iversen SD, Mishkin M (1970) Perseverative interference in monkeys following selective lesions of the inferior prefrontal convexity. Exp Brain Res 11:376–386

Jaeger P, Gilman S, Aldridge W (1993) Primate basal ganglia activity in a precued reaching task: preparation for movement. Exp Brain Res 95:51–64

Jahanshahi M, Brown RG, Marsden CD (1993) A comparative study of simple and choice reaction in time in Parkinson's, Huntington's and cerebellar disease. J Neurol Neurosurg Psychiatry 56:1169–1177

Jahanshahi M, Jenkins IH, Brown RG, Marsden CD, Passinham RE, Brooks DJ (1995) Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. Brain 118:913–933

Jeannerod M (1994) The representing brain: neural correlates of motor intention and imagery. Behav Brain Sci 17:187–246

Jeannerod M (1995) Mental imagery in the motor context. Neuropsychologia 33:1419–1432

Jeannerod M (1997) The cognitive neuroscience of action. Blackwell, Oxford

Jeannerod M, Arbib MA, Rizzolatti G, Sakata H (1995) Grasping objects: the cortical mechanism of visuomotor transformation. Trends Neurosci 18:314–320

Johnson PB, Ferraina S, Bianchi L, Caminiti R (1996) Cortical networks for visual reaching: physiological and anatomical organization of frontal and parietal lobe arm regions. Cereb Cortex 6:102–118

Jueptner M, Stephan KM, Frith CD, Brooks DJ, Frackowiak RSJ, Passingham RE (1997) Anatomy of motor learning. I. Frontal cortex and attention to action. J Neurophysiol (in press)

Kalaska JF, Crammond DJ (1995) Deciding not to GO: neuronal correlates of response selection in a GO/NOGO task in primate premotor and parietal cortex. Cereb Cortex 5:1047–3211

Kawashima R, Roland P, O'Sullivan BT (1994) Fields in human motor areas involved in preparation for reaching, actual reaching, and visuomotor learning: a positron emission tomography study. J of Neuroscience 14:3462–3474

Kurata K (1993) Premotor cortex of monkeys: set- and movement-related activity reflecting amplitude and direction of wrist movements. J Neurophysiol 69:187–200

Kurata K, Hoffman DS (1994) Differential effects of muscimol microinjection into dorsal and ventral aspects of the premotor cortex of monkeys. J Neurophysiol 71:1151–1164

Leonardo M, Fieldman J, Sadato N, Campbell G, Ibanez B, Cohen L, Deiber MP, Jezzard P, Pons T, Turner R, Le Bihan D, Hallet M (1995) A functional magnetic resonance imaging study of cortical regions associated with motor task execution and motor ideation in humans. Hum Brain Mapp 3:83–92

Luppino G, Matelli M, Camarda RM, Gallese V, Rizzolatti G (1991) Multiple representations of body movements in mesial area 6 and the adjacent cingulate cortex: an intracortical microstimulation study in the macaque monkey. J Comp Neurol 311:463–482

Matelli M, Luppino G, Rizzolatti G (1985) Patterns of cytochrome oxidase activity in the frontal agranular cortex of the macaque monkey. Behav Brain Res 318:125–137

Matelli M, Camarda R, Glickstein M, Rizzolatti G (1986) Afferent and efferent projections of the inferior area 6 in the macaque monkey. J Comp Neurol 251:281–298

Matsuzaka Y, Aizawa H, Tanji J (1992) A motor area rostral to the supplementary motor area (presupplementary motor area) in the monkey: neuronal activity during a learned motor task. J Neurophysiol 68:653–662

McCarthy G, Puce A, Constable RT, Krystal JH, Gore JC, Goldman-Rakic P (1996) Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functiona MRI. Cereb Cortex 6:600–611

Mink JW, Thach WT (1991a) Basal ganglia motor control. I. Nonexclusive relation of pallidal discharge to five movement modes. J Neurophysiol 65:273–300

Mink JW, Thach WT (1991b) Basal ganglia motor control. III. Pallidal ablation. Normal reaction time, muscle cocontraction, and slow movement. J Neurophysiol 65:330–351

Mitz AR, Zeffiro T, Wise SP (1993) Premotor cortex and the selection of actions. Soc Neurosci Abstr 19:496.9

Mushiake H, Strick PL (1993) Preferential activity of dentate neurons during limb movements guided by vision. J Neurophysiol 70:2660–2664

Mushiake H, Strick PL (1995a) Cerebellar and pallidal activity during instructed delay periods. Soc Neurosci Abstr 21:170.1

Mushiake H, Strick PL (1995b) Pallidal neurone activity during sequential arm movements. J Neurophysiol 74:2754–2758

Nixon PD, Passingham RE (1996) Lesions of the cerebellar nuclei impair sequence learning in a serial reaction-time task. Soc Neurosci Abstr 22:546.14

Oldfield RC (1971) The assessment and analysis of handedness. The Edinburgh inventory. Neuropsychologia 9:97–113

Pardo JV, Pardo PJ, Janer KW, Raichle ME (1990) The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. Proc Natl Acad Sci USA 87:256–259

Parsons LM, Fox PT, Hunter Downs J, Glass T, Hirsch TB, Martin CC, Jerabek PA, Lancaster JL (1995) Use of implicit motor imagery for visual shape discrimination as revealed by PET. Nature 375:54–58

Passingham RE (1993) The frontal lobes and voluntary action. (Oxford psychology, series, 21). Oxford University Press, Oxford

Passingham RE, Nixon PD (1996) Lesions of the cerebellar nuclei do not impair the acquisition of a visual-motor conditional learning task. Soc Neurosc Abstr 22:116.1

Paus T, Petrides MJ, Evans AC, Meyer E (1993) Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. J Neurophysiol 70:453–469

Paus T, Tomaiuolo F, Otaky N, MacDonald D, Petrides M, Atlas J, Morris R, Evans AC (1996) Human cingulate and paracingulate sulci: pattern, variability, asymetry, and probabilistic map. Cereb Cortex 6:207–214

Pellegrino G di, Wise SP (1991) A neurophysiological comparison of three distinct regions of the primate frontal lobe. Brain 114:951–978

Pellegrino G di, Wise SP (1993) Visuospatial versus visuomotor activity in the premotor and prefrontal cortex of a primate. J Neurosci 13:1227–1243

Pellegrino G di, Fadiga L, Fogassi L, Gallese V, Rizzolatti G (1992) Understanding motor events: a neurophysiological study. Exp Brain Res 91:176–180

Petrides M, Pandya DN (1994) Comparative architectonic analysis of the human and the macaque frontal cortex. In: Boller F, Grafman J (eds) Handbook of neuropsychology, vol 9. Elsevier, Amsterdam

Picard N, Strick PL (1996) Motor areas of the medial wall: a review of their location and functional activation. Cereb Cortex 6:342–353

Porro CA, Francescato MP, Cettolo V, Diamond M, Baraldi P, Zuiani C, Bazzochi M, di Prampero PE (1996) Primary motor and sensory cortex activation during motor performance and mental imagery: a functional magnetic resonance imaging study 16:7688–7698

Posner MI, Walker JA, Friedrich FJ, Rafal RD (1984) Effects of parietal injury on covert orienting of attention. J Neurosci 4:1863–1874

Preuss TM (1995) The argument from animals to humans in cognitive neuroscience. In: Gazzaniga M (ed) The cognitive neurosciences. MIT Press, Cambridge, Mass

Rao SM, Binder JR, Bandettini PA, Hammecke TA, Yetkin FZ, Jesmanowicz A, Lisk LM, Morris GL, Mueller WM, Estkowski LD, Wong EC, Haughton VM, Hyde JS (1993) Functional magnetic resonance imaging of complex human movements. Neurology 43:2311–2318

Riehle A, Requin J (1995) Neuronal correlates of the specification of movement direction and force in four cortical areas of the monkey. Behav Brain Res 70:1–13

Rizzolatti G, Matelli M, Pavesi G (1983) Deficits in attention and movement following the removal of postarcuate (area 6) and prearcuate (area 8) cortex in macaque monkeys. Brain 106: 655–673

Rizzolatti G, Camarda R, Fogassi L, Gentilluci M, Luppino G, Matelli M (1988) Functional organization of inferior area 6 in the macaque monkey. II. Area F5 and the control of distal movements. Exp Brain Res 71:491–507

Rizzolatti G, Fadiga L, Gallese V, Fogassi L (1996a) Premotor cortex and the recognition of motor actions. Cogn Brain Res 3:131–141

Rizzolatti G, Fadiga L, Matelli M, Bettinardi V, Paulesu E, Perani D, Fazio F (1996b) Localization of grasp representations in humans by PET. 1. Observation versus execution. Exp Brain Res 111:246–252

Romo R, Schultz W (1992) Role of the primate basal ganglia and frontal cortex in the internal generation of movements. II. Neuronal activity in the supplementary motor area. Exp Brain Res 91:396–407

Roth M, Decety J, Raybaudi M, Massarelli R, Delon-Martin C, Segebarth C, Morand S, Gemignani A, Decorps M, Jeannerod M (1996) Possible involvement of primary motor cortex in mentally simulated movement: a functional magnetic resonance imaging study. Neuroreport 7:12820–12824

Rushworth MFS, Nixon PD, Eacott MJ, Passingham RE (1997a) Ventral prefrontal cortex is not essential for working memory. J Neurosci 17:4829–4838

Rushworth MFS, Nixon PD, Renowden S, Wade DT, Passingham RE (1997b) The left parietal cortex and motor attention. Neuropsychologia 35:1261–1273

Rushworth MFS, Nixon PD, Renowden S, Wade DT, Passinghma RE (1998) The left hemisphere and the selection of learned actions. Neuropsychologia. 36:11–24

Sabbah P, Simond G, Levrier O, Habib M, Traband V, Murayama N, Mazoyer BM, Braint JF, Rabaud C, Salamon G (1995) Functional magnetic resonance imaging at 1.5 T during sensory, motor and cognitive tasks. Eur Neurol 35:131–136

Sanes JN, Stern CE, Baker JR, Kwong KK, Donoghue JP, Rosen BR (1993) Human frontal motor cortical areas related to motor performance and mental imagery. Soc Neurosci Abstr 18:1208

Sarkissov SA, Filimonoff JN, Kononova EP, Preobraschenskaja IS, Kukuew LA (1995) Atlas of the cytoarchitectonics of the human cerebral cortex. Medzig, Moscow

Savaki HE, Kennedy C, Sokoloff L, Mishkin M (1993) Visually guided reaching with the forelimb contralateral to a "blind" hemisphere: a metabolic mapping study in monkeys. J Neurosci 13:2772–2789

Schultz W, Romo R (1992) Role of primate basal ganglia and frontal cortex in the internal generation of movements. I. Preparatory activity in the anterior striatum. Exp Brain Res 91:363–384

Sheliga BM, Riggio L, Rizzolatti G (1994) Orienting of attention and eye movements. Exp Brain Res 98:507–522

Shima K, Aya K, Mushiake H, Inase M, Aizawa H, Tanji J (1991) Two movement related foci in the primate cingualate cortex observed in signal-triggered and self-paced forelimb movements. J Neurophysiol 65:188–202

Smyrnis N, Taira M, Ashe J, Georgopoulos AP (1992) Motor cortical activity in a memorized delay task. Exp Brain Res 92:139–151

Stephan KM, Fink GR, Passingham RE, Silbersweig D, Ceballos-Baumann AO, Frith CD, Frackowiak RSJ (1995) Functional anatomy of the mental representation of upper extremity movements in healthy subjects. J Neurophysiol 73:373–386

Talairach J, Tournoux P (1988) Co-planar Stereotaxic Atlas of the Human Brain. Thieme, Stuttgart

Taylor SF, Kornblum S, Minoshima S, Olivers LM, Koeppe RA (1994) Changes in medial cortical blood flow with a stimulus-response compatibility task. Neuropsychologia 32:249–255

Thach WT (1978) Correlation of neural discharge with pattern and force of muscular activity, joint position, and direction of intended next movement in motor cortex and cerebellum. J Neurophysiol 41:654–676

Thaler D, Chen Y, Nixon PD, Stern C, Passingham RE (1994) The functions of the medial premotor cortex (SMA). I. Simple learned movements. Exp Brain Res 102:445–460

Von Bonin G, Bailey P (1947) The neocortex of *Macaca mulatta.* University of Illinois Press, Urbana

Von Economo C (1929) The cytoarchitectonics of the human cerebral cortex. Oxford University Press, London

Weinrich M, Wise SP (1982) The premotor cortex of the monkey. J Neurosci 2:1329–1345

Weinrich M, Wise SP, Mauritz K-H (1984) A neurophysiological study of the premotor cortex in the rhesus monkey. Brain 107:385–414

Wilson FAW, Scalaidhe SPO, Goldman-Rakic PS (1993) Dissociation of object and spatial processing domains in primate prefrontal cortex. Science 260:1955–1957

Wise SP, Mauritz K-H (1985) Set-related neuronal activity in the premotor cortex of rhesus monkeys: effect of changes in motor set. Proc R Soc Lond B Biol Sci 223:331–354

Wise SP (1996) Evolution of neuronal activity during conditional motor learning. In: Bloedel JR, Ebner TJ, Wise SP (eds) The acquisition of motor behaviour in vertebrates. MJT, Cambridge Mass

Wise SP, Pelligrino GD, Boussaoud D (1998) The premotor cortex and non-standard sensorimotor mapping. Can J Physiol Pharmacol 74:469–482